CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA
GLUTARALDEHYDE

Chemical Code # 00139, Tolerance # 50255
SB 950 # 065

JULY 18, 2000
Revised January 19, 2001

I. DATA GAP STATUS

Chronic, rat:	No data gap, possible adverse effect (oral route)
Chronic toxicity, dog:	Data gap, no study submitted (acceptable subchronic oral study with no adverse effect)
Oncogenicity, rat:	No data gap, possible adverse effect (oral route)
Oncogenicity, mouse:	Data gap, inadequate study, no adverse effect indicated (inhalation) (acceptable oral subchronic study on file)
Reproduction, rat:	No data gap, no adverse effect
Teratology, rat:	No data gap, no adverse effect
Teratology, rabbit:	No data gap, no adverse effect
Gene mutation:	No data gap, possible adverse effect
Chromosome effects:	No data gap, possible adverse effect
DNA damage:	No data gap, no adverse effects
Neurotoxicity:	Not required at this time.

Toxicology one-liners are attached.

All record numbers through 178369 were examined.
** indicates an acceptable study.
Bold face indicates a possible adverse effect.
Original: H, Green, J. Kishiyama and J. Gee; revised by Gee, January 19, 2001
File name: T010119

These pages contain summaries only. Individual worksheets may contain additional effects.
Glutaraldehyde is an antimicrobial.

II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

COMBINED, RAT

123 098788 "Glutaraldehyde - Preliminary Results of a Chronic Toxicity/Oncogenicity Study", (Lab not identified, 10/4/91). Glutaraldehyde, administered in the drinking water at concentrations of 0, 50, 250 or 1000 ppm was given to 100 Fisher rats/sex/group with sacrifices of 10/sex/group at weeks 52 and 78 and to the remainder, for 104 weeks. Doses were equivalent to 0, 3.6, 17.1 and 63.9 mg/kg for males and 0, 5.5, 25.1 and 85.9 mg/kg/day for females. No ophthalmology was reported. Histopathology did not indicate treatment-related effect(s) from glutaraldehyde in drinking water. **Possible adverse effect reported: increased incidence of large granular cell lymphocytic leukemia primarily in liver and spleen for females in all glutaraldehyde dose groups.** As of 1991, the investigators were analyzing this as a possible modulating effect of a spontaneously occurring tumor in Fisher 344 rats. The information/report and study review is not complete and considered a "Draft". The draft was submitted as an adverse effects disclosure. The final report needs to be submitted for review. (Kishiyama and Gee, 8/3/99). [NOTE: See 50255-231 178363 below.]

**** 50255-231 178363** "Glutaraldehyde: Combined chronic toxicity/oncogenicity study in the drinking water of rats." (S. J. Hermansky and K. A. Loughran, Bushy Run Research Center, Union Carbide, ID 91U0012, March 18, 1994) Fischer 344 rats, 100/sex/dose, were given glutaraldehyde (UCARCIDE 250) in drinking water at 0, 50, 250 or 1000 ppm for 104 weeks. There were interim sacrifices of 10/sex/group at 52 and 78 weeks with the remaining survivors sacrificed at 104 weeks. Acceptable parameters for hematology, clinical chemistry, urinalysis and ophthalmology were examined. At 250 and 1000 ppm, the intake of water was significantly decreased with subsequent effects on urine volume and osmolality. Body weights were also decreased at the mid and, especially, at the high dose. There was evidence of gastric irritation at 250 and 1000 ppm, as early as 52 weeks. The lesions included multifocal color change, thickening of the wall and ulceration of the mucosa. Systemic NOEL = 50 ppm (gastric irritation). The major finding was a statistical increase in the incidence of large granular lymphocyte (LGL) leukemia in all doses in females (but not in males) when compared with concurrent controls. The overall incidences for all females was: 24, 41*, 41* and 53** per 100 animals. Although LGL leukemia is a common and spontaneous neoplasm in Fischer 344 rats, a role of glutaraldehyde could not be discounted. Possible adverse effect. ACCEPTABLE. (Gee, 1/12/01) Note: This study was reviewed as a draft report in 098788, 8/3/99. No definitive conclusions were made from the draft report.

Subchronic:

150 131903 Van Miller, J. P. " Glutaraldehyde: Ninety-Day Inclusion in Drinking Water of Rats". (Bushy Run Research Center, Project Report 48-107. December 13, 1985). Technical grade Ucarcide® 250 Antimicrobial (51.1% glutaraldehyde) was administered at concentrations of 0, 50,

250, or 1000 ppm (w/w corrected for percent active ingredient) for 13 weeks in the drinking water of 20 Fisher 344 rats/sex/group. Doses were equivalent to 0, 5, 25 and 100 mg/kg body weight for males and 0, 7, 35 and 120 mg/kg for females. Ten extra rats/sex in the control and high dose groups were observed for recovery in 4 weeks. There were no clinical findings reported. Water consumption decrease was reported as a result of aversion to glutaraldehyde in the drinking water for mid and high dose groups. Food consumption decreased slightly for the high dose groups; body weight/gain decreased slightly for high dose males and kidney weight increased for mid and high dose females. Nominal NOEL = 50 ppm based on marginal effects on water intake and food consumption at 250 ppm from summary data. High dose animals were reported as having a rapid recovery. Only summary tables were submitted and a full evaluation of the study could not be performed. UNACCEPTABLE (appendices of individual data and pathology report are missing). Upgradeable with submission of the missing appendices. (Kishiyama and Gee, 8/24/99). See 1-liner below. (Gee, 1/11/01)

** 150, 232 131903, 178364 The supplemental submission in record no. 178364 contains the appendices requested in the original review of 8/24/99. With these appendices containing histopathology and individual data, the study is upgraded to ACCEPTABLE status with a NOEL of 50 ppm (water and food consumption) with no adverse effects based on clinical parameters or histopathology. (Gee, 1/11/01)

149 131901 Kari, F. W. "Subchronic Inhalation Studies on Glutaraldehyde to F344/N Rats and B6C3F_1 Mice". (Battelle Northwest Laboratories for National Toxicology Program, RTP, NTP Toxicity Report No. 25, NIH Publication 93-3348. March 1993). Glutaraldehyde - 50% aqueous solution was administered as an inhalable vapor at concentrations of 0, 62.5, 125, 250, 500, or 1000 ppb to 10 F344/N rats and 10 B6C3F_1 mice/sex/group. Exposure period was 6.5 hours/day, 5 days/week for 13 weeks. Also included was a 2-week study with a total of 12 exposures at concentrations of 0.16 to 16 ppm (16,000 ppb). There were 5/sex/group. In the 13-week study, rats and mice became emaciated at the highest dose and mortality increased to 100% for high dose mice. Segmented neutrophils and leukocytes were significantly increased for high dose rats; and ALT and ALP increases were noted for rats in 250 ppb and higher groups. Body weight was reduced in the two highest and the four highest rat and mice groups, respectively. **Possible adverse effects:** Lesions in the respiratory tract of rats and mice were extensive at the highest dose and present but less extensive at lower dosages. **TWO week** study: RATS: NOEL = 160 ppb (nasal hyperplasia and metaplasia at 500 ppb); other affects were mortality at 5 and 16 ppm, lower body weight and histopathology of nasal passages and larynx (both sexes) at 1.6 ppm. MICE: NOEL = 0.5 ppm [500 ppb] (mortality and histopathology finding in nasal passages and larynx at 1.6 ppm; all mice died at 1.6, 5 and 16 ppm. **THIRTEEN weeks** study: RATS: NOEL = 125 ppb (decreased body weight, respiratory tract effects). MICE: NOEL < 62.5 ppb (inflammation of anterior nasal passage at all doses. UNACCEPTABLE (insufficient information: no individual data, no ophthalmology, no hematology or clinical chemistry in mice). Not upgradeable. (Kishiyama and Gee, 8/6/99)

233 178365 Duplicate of 149 131901 (Gee, 1/11/01)

** 147 131899 Werley, M. S. and C. L. Benson. **"**Glutaraldehyde: Twenty-Eight Day Repeated Cutaneous Dose Toxicity Study in Fischer 344 Rats" (Bushy Run Research Center, Laboratory

Project ID 93U1252, May 26, 1994.) Ucarcide® 250 Antimicrobial (glutaraldehyde) aqueous solutions of 2.5, 5.0, or 7.5%, 2 ml/kg, equivalent to 50, 100, or 150 mg/kg/day were administered via occluded skin (6 hours/day for 20 days) to 15 rats/sex (control and high dose groups) and 10 rats/sex (low and mid-dose groups). Five control and high dose rats/sex were held after treatment for an additional 4-week recovery period. Body weight gain was reduced during the first 4 days of treatment and later (day 15-22) food reduction was noted for high dose males. No treatment-related systemic effects reported. Erythema was "barely perceptible" but the onset and incidence appeared dose related. The treated area of the skin had signs of desquamation/exfoliation, excoriation, crusting and skin necrosis. Microscopic evaluation detected skin lesions which were reported as superficial (acanthosis, dermatitis, dermal fibrosis, and hyperkeratosis/parakeratosis) and secondary due to skin irritation and binding. Animals at the end of the recovery period showed minimal to no secondary effects. Dermal NOEL < 2.5%glutaraldehyde or 50 mg/kg body weight/day (skin changes at all doses). ACCEPTABLE. (Kishiyama and Gee, 7/17/2000).

CHRONIC TOXICITY, DOG

No study on file.

Subchronic:

** 148 131900 Williams, K. D. " Glutaraldehyde: 13-Week Toxicity Study in Dogs with Administration Via the Drinking Water." (Hazleton Laboratories America, Inc. Project ID: HLA 6214-104. November 17, 1989). Glutaraldehyde, 50% a.i., was administered at concentrations of 0, 50, 150, and 250 ppm (Males: 3.3, 9.6 and 14.1 mg/kg and females: 3.2, 9.9 and 15.1 mg/kg) for 13 weeks in the drinking water of 4 Beagle dogs/sex/group. Food- and fluid-like vomitus were observed in all groups, but were more frequent in mid and high dose groups. Body weight was reduced at least 10% for mid and high dose females [initial body weights, however, were 6 and 4% lower at week 0, respectively] and cumulative change in bodyweight at least 28% lower for all female groups. Food and water consumption of females was slightly lower at 250 ppm. In males, food and water consumption values were reduced 28% and 51%, respectively and statistically significant only during week 2 for high dose males. Kidney weight increase was reported as treatment related, but not toxicologically important since there was no evidence of toxicity from histopathology or clinical chemistry/urinalysis data. The significance of ovary weight increase was reported as unclear. Overall, the NOEL = 50 ppm, based on lower body weights, primarily in female dogs, at the mid dose. ACCEPTABLE with no adverse effect. (Kishiyama and Gee, 8/4/ 99)

ONCOGENICITY, RAT

50255-234 178366 "Toxicology and carcinogenesis studies of glutaraldehyde (CAS No. 111-30-8) in F344/N rats and $B6C3F_1$ mice [RATS]" (National Toxicology Program, NTP No. 490, NIH Publication No. 99-3980, Battelle Northwest Laboratories, B. J. Chou, Principal Investigator, September, 1999) F344/N rats, 50/sex/group, were exposed to glutaraldehyde by whole-body inhalation at doses of 0, 250, 500 and 750 ppb, 6 hours/day plus T_{90} (25 minutes), 5 days/week, for

104 weeks. No hematology, clinical chemistry, urinalysis and ophthalmology were included in the study. Body weights but not food consumption were recorded but no individual data were included. Nonneoplastic effects of glutaraldehyde were noted in the examination of the nose. Four sections (an added section of level I) were examined for all males and females. Lesions were most common and severe in the squamous epithelium of level I with lower incidence and severity in the second section (respiratory epithelium), infrequent in level III and rare in level IV. Lesions in the squamous epithelium were hyperplasia and inflammation. Incidences were for hyperplasia: males, 3, 11*, 39** and 48** of 50 examined; females, 3, 15**, 29** and 45**. For inflammation, males, 6, 17*, 41** and 49**; females, 6, 26**, 42** and 48**. At 500 and 750 ppb, both sexes showed evidence of effects in the respiratory epithelium and olfactory epithelium. Sys. NOEL < 250 ppb (nasal effects). There was no evidence of oncogenicity reported. The study was considered unacceptable based on the lack of individual data, organ weights and blood smears. UNACCEPTABLE as an oncogenicity study. Questionable if upgradeable. (Gee, 1/17/01)

ONCOGENICITY, MOUSE

50255-234 178366 "Toxicology and carcinogenesis studies of glutaraldehyde (CAS No. 111-30-8) in F344/N rats and B6C3F_1 mice [MICE]." (National Toxicology Program, NTP No. 490, NIH Publication No. 99-3980, Battelle Northwest Laboratories, B. J. Chou, Principal Investigator, September, 1999) B6C3F_1 mice, 50/sex/dose, were exposed to glutaraldehyde (25% aqueous solution) by whole-body inhalation to 0, 62.5, 125 and 250 ppb, 6 hours plus T_{90} (25 minutes) per day, 5 days per week, 104 weeks. No hematology, clinical chemistry, urinalysis and ophthalmology were conducted. No blood smears or organ weights were taken. Body weights were collected buy only mean data were provided in the report. Four sections (an added section of level I) of the nose of all animals were examined. Female mice were more severely affected than males with all groups showing increased incidence of hyaline degeneration of the respiratory epithelium. Squamous metaplasia was also increased in females at 125 and 250 ppb and in males at 250 ppb. Systemic NOEL < 62.5 ppb (effects on respiratory epithelium). No evidence of oncogenicity. UNACCEPTABLE (missing data). Questionable if upgradeable. (Gee, 1/17/01).

Subchronic:

See also 149 131901 above under combined rat.

** 150 131904 Gill, M. W. and J. P. Van Miller. "Glutaraldehyde: Ninety-Day Drinking Water Toxicity Study in Mice." (Bushy Run Research Center, Laboratory Project ID 52-1, March 20, 1989) Glutaraldehyde as a 25.9% aqueous solution with >99% purity of glutaraldehyde was administered at concentrations of 0, 100, 250 or 1000 ppm (w/w) for 13 weeks in the drinking water of 20 CD-1® mice/sex/group. Ten extra mice in control and high dose groups served as a recovery group of six weeks. Doses were equivalent to 25, 61 and 200 mg/kg/day for males and 31, 74 and 238 mg/kg/day for females. Water consumption decreased for the high dose groups; urinalysis indicated osmolality increased for the high dose group and urine volume decreased for mid and high dose males and high dose females; however, these effects were absent during the recovery period. There were no clinical

signs, effects on hematology, clinical chemistry, ophthalmology or histopathology. NOEL = 100 ppm based on marginal effects at 250 ppm on urine volume. No adverse effects were noted at 1000 ppm other than decreased water consumption, reported as due to palatability. ACCEPTABLE. (Kishiyama and Gee, 8/25/99)

REPRODUCTION, RAT

** 146 131898: Chun, J. S. and T. L. Neeper-Bradley, "Glutaraldehyde: Two-Generation Reproduction study in the Drinking Water of CD7 Rats". (Bushy Run Research Center, Lab Project ID 92U1059, 3/24/94.) Glutaraldehyde (Ucarcide® Antimicrobial 250), purity 51% glutaraldehyde, at concentrations of 0, 50, 250 or 1000 ppm in the drinking water during two generations, 28 albino CD® rats/sex/group. Water consumption decreased (considered an aversion affect) up to 15-20% and 25-35% throughout dosing for mid and high dose groups and on occasion 9-11% for low dose females. Other treatment-related effects reported were reduced food consumption up to 9-10% for high dose groups and reduced body weight gain without an apparent similar affect on body weight for F0 mid and high dose groups; Adult NOEL = 50 ppm. Body weight of F1 and F2 high dose pups decreased 5-7% during lactation Day 21; Pup NOEL = 250 ppm Reproductive NOEL = >1000 ppm. ACCEPTABLE. (Kishiyama and Gee, 7/17/2000)

TERATOLOGY, RAT

** 133 114688 "Study of The Prenatal Toxicity of Glutaraldehyde in Rats after Oral Administration (Drinking Water)", (J. Hellwig & B. Hildebrand, BASF Aktiengesellschaft, Project 33R0599/89025, 2/11/91). Glutaraldehyde, 50.3% a.i., was administered in the drinking water at concentrations of 0, 50, 250 or 750 ppm to 25 pregnant Wistar female rats/group during Days 6 to 16 post coitum. Mean doses were approximately 5, 26 and 68 mg/kg/day. Water consumption was reduced/averted 19% and 12% for high and mid dose groups, respectively. Body weight and weight gain were not affected. Maternal NOEL = 50 ppm/day, based on reduced water consumption. There were no clinical or necropsy findings due to treatment. No malformations or variations reported; Developmental NOEL = 750 ppm/day. Doses and route of administration were based on two range-finding studies using gavage and drinking water. Comparison of the results indicated that a high dose could be delivered by drinking water. ACCEPTABLE with no systemic effects. (Kishiyama and Gee, 8/2/99).

TERATOLOGY, RABBIT

** 132 114685 Hellwig, J. and B. Hildebrand. "Study of The Prenatal Toxicity of Glutaraldehyde in Rabbits after Oral Administration (Gavage)". (BASF Aktiengesellschaft, Project 40R0599/89026, 2/11/91). Glutaraldehyde, 50.3% a.i., was administered via gavage at concentrations of 0, 5, 15 or 45 mg/kg/day to 15 presumed-pregnant Himalayan female rabbits/group during Days 7 through 19 post insemination. The study was divided into three sections (5 females/group/section; 7 days' laps between sections). Maternal effects at 45 mg/kg/day: increased mortality (5/15) and total resorption

(in 9/10 of surviving dams); reduced body weight (10-21%) and food consumption (69-99%), clinical signs. Fetal weight was reduced 36% for the high dose group. Maternal and developmental NOEL = 15 mg/kg/day. No adverse developmental was identified in the absence of maternal toxicity. ACCEPTABLE. (Kishiyama and Gee, 7/30/99).

TERATOLOGY, MOUSE

043 034346 "Influence of formaldehyde and Sonacide (potentiated acid glutaraldehyde) on embryo and fetal development in mice." (Research Triangle Institute, 2/2/80; published in: *Teratology* 22: 51 - 58 (1980)) CD-1 mice, 11 to 24 pregnant mice per group, were given glutaraldehyde (2% plus 98% inerts) by gavage at 0 (water), 0.8, 1.0, 1.2, 2.0, 2.5 or 5.0 mg/kg/day, days 6 - 15 of gestation. There were 6, 12 and 19 deaths at 2, 2.5 and 5 mg/kg, respectively, during the study. Many of the initial number of animals were not pregnant: 86/101 for controls; 11/26 at 0.8; 11/35 at 5.0 mg/kg, for example. Animals were sacrificed on day 18 with 1/3 of fetuses per litter given a visceral exam and all fetuses examined for skeletal affects. Nominal maternal NOEL = 1.2 mg/kg (mortality), nominal developmental NOEL = 2.5 mg/kg (lower fetal weight, increased resorptions and stunted fetuses at 5 mg/kg). UNACCEPTABLE (no individual data for dams or fetuses, no dosing analysis, no historical control data.) Possibly upgradeable with full study. (Parker, 9/17/85, 1-liner by Gee, 7/22/99).

028, 031, 035, 017649, 028374, 040199, Journal article - see above.

006 031779 Brief summary.

GENOTOXICITY

237 178369 "Mutagenicity studies with glutaraldehyde: Summary of genotoxicity studies." (B. Ballantyne, Union Carbide Corporation, CT, 12/2/92) This report is not a study but a summary of a number of studies of genotoxicity with a variety of cells *in vitro* and with animals *in vivo*. The author has listed the studies in table form with an interpretation of the results as negative, positive, weak positive, no activity, and slight activity. (Gee, 1/11/01)

GENE MUTATION

**** 145 131240**: Stankowski, L.. "Ames/*Salmonella* Plate Incorporation Assay on Sepacid GA 50". (Pharmakon Research International, PH 301-BS-001-093, 5/18/94). Sepacid GA 50, 50.2% a.i., at concentrations of 0, 0.50, 1.67, 5.0, 16.7, 50 and 100 µg/plate, with and without metabolic activation (S9 Mix), was evaluated for mutagenicity after 48 hours exposure using *Salmonella typhimurium* strains, TA98, TA100, TA102, TA104, TA1535, TA1537 and TA1538. **Adverse effect: the increase in revertant frequency** was confirmed in a repeat assay on *Salmonella typhimurium* strains TA98, TA100 (marginal), TA102 and TA104 with S9 Mix and TA100 (marginal), TA102 and TA104 without S9 Mix. ACCEPTABLE. (Kishiyama and Gee, 7/21/2000).

149 131901 Kari, F. W. "Subchronic Inhalation Studies on Glutaraldehyde to F344/N Rats and B6C3F_1 Mice"; **Section: Analysis of Mutagenicity in *Salmonella typhimurium*.** (National Toxicology Program, RTP, NTP Toxicity Report No. 25, NIH Publication 93-3348. March 1993. Assays were conducted in three laboratories) Glutaraldehyde (purity not given) was evaluated for mutagenicity with and without metabolic activation at concentrations ranging from 0 to 333 µg/plate (EG&G Mason Research Institute) and 0 to 3333 µg/plate (Case Western Reserve University) using *Salmonella typhimurium* strains TA100, TA1535, TA1537, and TA 98; and 0 to 300 µg/plate using *Salmonella typhimurium* strains TA100, TA102, and TA104 (Inversek Research International). A 20 minute preincubation was used before plating and a further incubation period of two days. **Marginal increase in revertants we re observed with *S. typhimurium* TA 100 (EG&G Mason Research) and TA 100, TA 102 and TA104 (Inversek International) with and without metabolic activation in initial and repeat trials.** Other strains gave negative results. UNACCEPTABLE. Insufficient information. Possibly upgradeable with)submission of the full report of methods and individual data. (Kishiyama and Gee, 8/19/99)

234 178366 Same data as in 131901 for *Salmonella*. (Gee, 1/17/01).

** 131 114673 Hengler, W. C. and R. S. Slesinski. "Glutaraldehyde *Salmonella*/Microsome (Ames) Bacterial Mutagenicity Assay". (Bushy Run Research Center, Intramural Project Report 44-131, 12/11/ 1981; reformatted by J. S. Vergnes, 5/21/90) Glutaraldehyde, 51.57%, lot # 7619-12A, at concentrations of 0 (distilled water), 0.0003, 0.001, 0.003, 0.01, 0.03 and 0.10 µl/plate without S9 Mix and at 0 (distilled water), 0.001, 0.003, 0.01, 0.03 and 0.10 µl/plate with S9 Mix was evaluated by plate incorporation for mutagenicity after 48-72 hours incubation using *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538. There were triplicate plates at each concentration and two trials. Glutaraldehyde was not mutagenic causing no significant increase in revertants. ACCEPTABLE with no positive response. (Kishiyama and Gee, 7/27/99).

131 114661 and 114672 same study as 114673 above.

**** 151 131905** Vergnes, J. S. and E. R. Morabit, "Ucarcide® Antimicrobial 250 (Glutaraldehyde, 50% aqueous solution): Mutagenic Potential in the *Salmonella*/Microsome (Ames) Assay". (Bushy Run Research Center (BRRC), Laboratory Project ID 92U1178. September 15, 1993). Ucarcide® Antimicrobial 250, 50% glutaraldehyde, at concentrations ranging from 0.003 to 0.3 mg/plate (spaced approximately at half-log intervals) in the presence and absence of S9 Mix was evaluated for potential mutagenicity using *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538, triplicate plates in two trials. In the repeat trial, concentrations were 0.003 to 0.1 mg/plate -S9 and 0.01 to 0.2 mg/plate + S9. Actual glutaraldehyde concentration was 50% of the values in the report. **Adverse effect: the number of revertant colonies increased for strain TA100 with 0.1 mg/plate Ucarcide â in the presence of S9 Mix and was confirmed in a repeat trial.** ACCEPTABLE. (Kishiyama and Gee, 7/14/2000).

50255 – 235 178367 "Report on the mutation test for glutaraldehyde." (T. Mizuno *et.al.*, Research and Development Department, Maruishi Pharmaceutical Company, Japan, circa 1980) *Salmonella typhimurium* strains TA98, TA100 and TA1537 were tested for activity with

glutaraldehyde (25% solution) at 0 (water), 1, 5, 10 or 50 ug/plate using a 20 minute pre-incubation step before plating. Cells were tested without and with activation of rat liver induced with sodium Phenobarbital and 5,6-benzoflavone. Formalin was tested at these same concentrations. Appropriate positive controls were used and were functional. Apparently, there was a single plate per concentration per strain. Results did not indicate induction of reversions. UNACCEPTABLE (inadequate number of strains and number of plates, no justification for concentrations used). Not upgradeable. (Gee, 1/11/01)

032 016877 "Mutagenicity of aldehydes in Salmonella" (Y. Sasaki and R. Endo, Tokyo Metropolitan Research Institute, in: *Mutation Research* 54: 251 - 252 (1978)) Glutaraldehyde was one of 19 aldehydes tested in *Salmonella typhimurium* strains TA100 and TA98. Bacteria were preincubated for 15 minutes with and without activation before plating. The abstract indicates that glutaraldehyde was negative. No worksheet. UNACCEPTABLE (abstract lacking in details.) (Gee, 7/23/99).

134 115342 Journal article.

**** 145 131241**, "AS52/XPRT Mammalian Cell Forward Gene Mutation Assay on Sepacid GA 50" (L. F. Stankowski, Jr., Pharmakon Research International, Inc., PH 314-BS-001-93, 5/24/94). Sepacid GA 50, 50.2% a.i., at concentrations ranging from 167 to 16,700 ng/ml with S9 Mix and 5 to 16,700 ng/ml without S9 Mix, was evaluated for mutagenicity in Chinese hamster ovary (CHO) cells. Cytotoxicity was observed at 2500 ng/ml without S9 Mix and at 16700 ng/ml with S9 Mix. **Adverse effect: Increased mutation frequency was confirmed in a repeat Assay.** ACCEPTABLE. (Kishiyama and Gee, 7/21/2000).

151 131906 Vergnes, J. S. "Ucarcide® Antimicrobial 250 (Glutaraldehyde, 50% aqueous solution): Mutagenic Potential in the CHO/HGPRT Forward Mutation Assay" (Bushy Run Research Center (BRRC), Laboratory Project ID 92U1179, April 8, 1994). Ucarcide® Antimicrobial 250, purity 50% glutaraldehyde, at concentrations ranging from 0.0003 to 0.03 and 0.001 to 0.10 mg/ml without and with S9 Mix, respectively, was evaluated for potential mutagenicity in cultured Chinese hamster ovary cells. UNACCEPTABLE. Excessive difference between duplicates of same concentration making interpretation difficult. Inconclusive results. (Kishiyama and Gee, 7/14/00).

149 131901 Kari, F. W. "Subchronic Inhalation Studies on Glutaraldehyde to F344/N Rats and B6C3F$_1$ Mice"; **Section: Mouse Lymphoma Mutagenicity Test**. (Inveresk Research International for National Toxicology Program, RTP, NTP Toxicity Report No. 25, NIH Publication 93-3348. March 1993.) Glutaraldehyde was evaluated for mutagenicity without metabolic activation at concentrations ranging from 0.5 to 16 µg/ml using Mouse Lymphoma L5178Y cells with exposure for 4 hours and a 48-hour expression period. Duplicate cultures were used and two trials were performed. Trifluorothymidine was used to select for mutants (TK -/-) **A positive response for mutagenicity was observed at the highest non-lethal dose (8 µg/ml) in both the initial and repeat trials**. Because of the positive response without activation, the assay was not repeated with activation. UNACCEPTABLE (report is incomplete with inadequate description of actual methods, no individual data and no activation included.) Not upgradeable. (Kishiyama and Gee, 8/20/99).

234 178366 Same data as 149 131901 on mouse lymphoma. (Gee, 1/17/01)

149 131901 Kari, F. W. "Subchronic Inhalation Studies on Glutaraldehyde to F344/N Rats and B6C3F$_1$ Mice"; **Section: *Drosophila melanogaster* sex-linked recessive lethal test**. (National Toxicology Program, RTP, NTP Toxicity Report No. 25, NIH Publication 93-3348. March 1993. Brown University) Glutaraldelyde (purity not stated) was given to male *Drosophila melanogaster* Canton-S wild-type flies by feeding for three days (3000 and 4000 ppm) or by a single injection (7500 and 10,000 ppm, 0.2 to 0.3 ul). Treated males were mated with 3 to 5 untreated female *Basc* strain flies to produce three matings of 3, 2 and 2 days. Results were reported as "No. of lethal/No. of X chromosomes tested." Deaths and sterility were also reported. The results were negative for production of sex-linked recessive lethals but significant death occurred at 4000, 7500 and 10000 ppm and some sterility was noted, especially at 4000 and 7500 ppm. UNACCEPTABLE (missing information regarding test material, methods). Results presented in summary form. Possibly upgradeable with full report. (Kishiyama and Gee, 8/23/99)

234 178366 Same data on *Drosophila* as in 149 131901. (Gee, 1/17/01).

131 114665, 114683 Slesinski, R.S. "Glutaraldehyde (50%) *In Vitro* Mutagenesis Studies: 3 Test Battery. Chinese Hamster Ovary (CHO) Mutation Test". Bushy Run Research Center, Project 43-16. 1/28/80. Summarized by J. S. Vergnes, 5/21/90. Glutaraldehyde, 50.7% ai, batch IS-189350, was tested at concentrations of 0, 0.5, 1.0, 2.0, and 4.0 x 10^{-4}% (v/v) without S9 and at 0, 0.0625, 0.125, 0.25, 0.5, and 1.0 x 10^{-4}% (v/v), five hour exposure followed by further incubation before determination of cytotoxicity. A single culture per concentration with four plates per concentration for mutant selection. Test #1 was repeated due to poor cell growth with S9 and high mutation frequency in the water control without activation. No statistically significant or consistent increase in mutation frequency was reported for Test #2. UNACCEPTABLE, not upgradeable (no independent repeat, only a single culture per concentration, no individual data, low % survival for solvent (water) control with activation in both trials). (Kishiyama and Gee, 7/23/99).

032 016887?? Same study as 131 114683.

032 016879. Same study as 131 114683. "Glutaraldehyde (50%) *In Vitro* Mutagenesis Studies: 3-Test Battery. CHO Mutation Test - Glutaraldehyde", (Ronald S. Slesinski, Ph.D., Chemical Hygiene Fellowship, Carnegie-Mellon Institute of Research, Carnegie-Mellon University, 4400 Fifth Avenue, Pittsburgh, PA. 15213, Report # 43-16, 1/28/80) (J. Berliner, 4/22/85)

131 114675 Slesinski, R. S. and P. J. Guzzie, "Glutaraldehyde (50%) *In Vitro* Mutagenesis Studies: CHO Mutation Test". (Bushy Run Research Center, Project 44-67, 6/23/81; Reformatted by J. S. Vergnes, 5/21/90). Glutaraldehyde, 51.57 %, at concentrations of 5 to 80 x 10^{-5} % (v/v) without S9 Mix and 10 to 100 x 10^{-5} % (v/v) with S9 Mix were evaluated for mutagenic potential on Chinese Hamster (CHO) ovary cells. Dose rates 50 to 80 x 10^{-5} % (v/v) without S9 and 60 to 100 x 10^{-5} % (v/v) were extremely toxic to CHO cells. Single trial with one culture per concentration. Unclear how many plates were used for survival determination. Protocol states that 4 plates per concentration were used for determination of mutation frequency. Glutaraldehyde was not mutagenic in CHO under test conditions. UNACCEPTABLE (single culture per concentration, no individual plate

counts, low survival with solvent controls). Not upgradeable. (Kishiyama and Gee, 7/27/99).

131 114670. Summary of 131 114675. (No worksheet). (Kishiyama and Gee, 7/27/99).

043 034347 "Mutagenicity Evaluation of Agrocide II Formula No. 3 Batch No. 10-582, in the Mouse Lymphoma Assay, Final Report" (David Brusick, Litton Bionetics, Inc., MD, Report # 2684, March, 1977) Agrocide II Formula No. 3, batch 10-582, Wavicide-05/06, purity not provided, was tested in the forward mutation assay with Fischer L5178Y mouse lymphoma cells in the presence and absence of activation (male mouse liver) with 5 hour exposure at non-activated concentrations of 0 (culture medium), 0.625, 1.25, 2.50, 5.0, 10.0, and 20.0 nl/ml and with activation at 0, 2.5, 5.0, 10.0, 20.0, 40.0, and 80.0 nl/ml. Bromodeoxyuridine was used to select for TK -/- mutants. Positive controls were ethylmethanesulfonate and dimethylnitrosamine. Colonies were not sized. Increased forward mutation frequency was not indicated. UNACCEPTABLE, not upgradeable (a confirmatory second trial was not performed). (D. Shimer and A. Apostolou, 9/17/85)

015, 031, 035, 044 026420, 028375, 040203, 034829, exact duplicates of record # 034347.

008 031809, 031810, 920354, brief results summary.

032 016879 Duplicate of records in 131, 114681, 114683 and 114663. See reviews under those record numbers (Gee, 7/23/99)

006 920372 Brief summary.

236 178368 “New forward mutation assay using low-concentration streptomycin resistance mutation in *E. coli* strains with plasmid pKM101” (M. Kosako and H. Nishioda, Laboratory of Biochemistry, Doshisha Univ., Japan, in: *The Science and Engineering Review of Doshisha University* 22: (1982)) Glutaraldehyde was one of a number of chemicals tested. Concentrations were 0 to 20 ug/plate, without activation. Mutation of resistance to streptomycin at 5 ug/ml was tested with *E. coli* WP 2uvrApKM 101. The chemical was incubated with the bacteria for 30 minutes, agar added and solidified followed by an overlay of soft agar containing streptomycin. After 4 days, SM^r-5 colonies were counted. Glutaraldehyde without activation increased the number of streptomycin-resistant colonies with concentration. Results with TA98 and TA100 were negative. Results were presented as figure 11. [Formaldehyde was also positive in this assay.] UNACCEPTABLE. Limited focus of the study was the verification of the assay. No worksheet. (Gee, 1/11/01).

CHROMOSOME EFFECTS

** 152 131909 Vergnes, J. S. and E. R. Morabit, "Ucarcide® Antimicrobial 250 (Glutaraldehyde, 50% aqueous solution): Bone Marrow Chromosomal Aberrations Assay in Rats" (Bushy Run Research Center (BRRC), Laboratory Project ID 91UO139, May 27, 1993). Ucarcide® Antimicrobial 250, purity 50%, was administered via a single peroral intubation at doses of 0, 25, 60, or 120 mg/kg to male rats and at 0, 15, 40, or 80 mg/kg to female rats. Dosing solutions were not adjusted for percent glutaraldehyde so the actual dose was approximately 2 of the stated mg/kg. Five

Sprague-Dawley rats/sex/group were sacrificed at 12, 24 and 48 hours after treatment. Cyclophosphamide at 24 hours was the positive control and was functional. Ucarcide® treatment did not increase chromosomal aberrations. ACCEPTABLE (Kishiyama and Gee, 8/26/99)

234 178366 "Toxicology and carcinogenesis studies of glutaraldehyde (CAS No. 111-30-8) in F344/N rats and B6C3F_1 mice " (National Toxicology Program, NTP No. 490, NIH Publication No. 99-3980, Battelle Northwest Laboratories, B. J. Chou, Principal Investigator, September, 1999) Section: **Chromosomal aberrations *in vivo* in male mice.** One page of data from a study performed at Environmental Health Research and Testing, Inc. Glutaraldehyde was given as a single intraperitoneal injection at 0 (saline), 15, 30, 50 and 60 mg/kg, 8 male mice per dose group. Mitomycin C, 1 mg/kg, was the positive control. Fifty first-division metaphases were scored per animal. In trial 1, a harvest time of 17 hours was used. No significant increase in aberrant cells was found. In trials 2 and 3, the harvest time was 36 hours. In both trials, a statistically significant increase in % aberrant cells was found, increasing in trial 2 with dose. The % aberrant cells (excluding gaps) was: control, 0.5%; 15 mg/kg, 1.5; 30 mg/kg, 3.25; 50 mg/kg, 5.25; 60 mg/kg, 5.75%, $p < 0.001$ by a one-tailed trend test. The results from trial 3 were not as clear with statistical significance only at 60 mg/kg. The study was UNACCEPTABLE because only a summary page of data was included with protocols by citation (page 00217). No worksheet. (Gee, 1/18/01).

** 131 114664 Vergnes, J. S. and E. R. Morabit. "Ucarcide® Antimicrobial 250 (Glutaraldehyde, 50% Aqueous Solution): *In Vitro* Chromosomal Aberrations Assay in Chinese Hamster Ovary Cells". (Bushy Run Research Center, Lab Project 54-101, 9/12/91) Ucarcide®, 50%, at concentrations of 0, 0.1, 0.3 and 1.0 ug/ml in the absence of S9 and at 1.0, 3.0 and 10 µg/ml in the presence of S9 was evaluated for mutagenicity potential using Chinese (CHO) hamster ovary cells. Cell survival was at least 80% for the highest dose evaluated (with or without S9 Mix). Higher concentrations were tested but not evaluated. Percent of aberrant cells (excluding gaps) did not increase significantly after 4 hours exposure to Ucarcide® dose levels (with and without S9 Mix) under the study conditions. Harvest time was at 10 hours after beginning of treatment, based on a cell cycle analysis. ACCEPTABLE with no indication of a genotoxic effect. (Kishiyama and Gee, 7/27/99)

**** 151 131907**: Vergnes, J. S. and E. R. Morabit, "Ucarcide® Antimicrobial 250 (Glutaraldehyde, 50% aqueous solution): Sister Chromatid Exchange Assay in Cultured CHO Cells". (Bushy Run Research Center (BRRC), Laboratory Project ID 92U1180. 4/7/94.) Ucarcide® Antimicrobial 250, purity 50.9% glutaraldehyde, at concentrations ranging from 0.00003 to 0.0003 mg/ml without S9 and 0.0001 to 0.003 mg/ml with S9 Mix was evaluated *in vitro* for genotoxic activity using Chinese hamster ovary (CHO) cells. The SCEs/chromosome values, although statistically significant were reported as not treatment related by the authors, since the increases were slight and not dose related. **However, there was a statistically**

significant increase of SECs/chromosome for the highest dose evaluated (0.001 mg/ml) in the presence of S9 Mix. ACCEPTABLE with a possible adverse effect with activation. (Kishiyama and Gee, 7/14/2000)

149 131901 Kari, F. W. "Subchronic Inhalation Studies on Glutaraldehyde to F344/N Rats and B6C3F_1 Mice"; **Section: Induction of Sister Chromatid Exchanges in Chinese Hamster Ovary Cells**. (Litton Bionetics, Inc. and Columbia University for the National Toxicology Program, RAP, N.T.P. Toxicity Report No. 25, NIH Publication 93-3348. March 1993.) Glutaraldehyde was evaluated for mutagenicity with and without metabolic activation at concentrations ranging from 0.36 to 30 µg/ml (Litton Bionetics, Inc.) and 0.5 to 16 µg/mL (Columbia University) using Chinese hamster ovary cells. Fifty or one hundred cells were scored per concentration. **Glutaraldehyde induced sister chromatid exchange with and without metabolic activation in Litton Bionetics, Inc., trials. Chromosome aberrations increased in the study at Columbia University (no repeat study).** UNACCEPTABLE (numerous deficiencies including lack of details for methods, identity of test material). (Kishiyama and Gee, 8/23/99).

234 178366 Same data on CHO as in 149 131901. (Gee, 1/17/01).

131 114681, 114667, 114663 Slesinski, R. S. "Glutaraldehyde (50%) *In Vitro* Mutagenesis Studies: 3 Test Battery, Determination of Sister Chromatid Exchange Frequencies in Chinese Hamster Ovary Cells *In Vitro*". (Bushy Run Research Center, Project 43-16, 1/28/80; Reformatted by J.S. Vergnes, 5/21/90). Glutaraldehyde technical, 50.7% ai., lot IS-189350, at concentrations of 0 (water), 0.0312, (only with S9 Mix), 0.0625, 0.125, 0.25, 0.5, and 1.0 x 10^{-4}% (v/v) with and without metabolic activation (S9 Mix) was evaluated for mutagenic potential using the Sister Chromatid Exchange (SCE) test. Glutaraldehyde with S9 Mix was toxic at the highest dose (1 x 10^{-4} % (v/v)) and at the second high dose (0.5 x 10^{-4}%) there was an increased SCE/chromosome which was reported as a "chance event". Record #114667 contains a statement that of the 15 cells scored at 0.5 x 10^{-4}%, 7 did not have a model number of $\pm$ 2 centromeres. Based on the deficiencies in scoring, the study is not considered to demonstrate a positive effect for sister chromatid exchange induction. UNACCEPTABLE (inadequate number of cells scored, model number of centromeres not considered, single culture per concentration, no repeat test, no individual data). Not upgradeable. (Berliner and Parker, 4/22/85; Kishiyama and Gee, 7/26/99)

032 016881 See review under 131 114681 above.

032 016878 "Mutagenicity of glutaraldehyde in mice" (Translation: M. Tamada, S. Sasaki, Y. Kadono, S. Kato, M. Amitani, Y. Ogasahara, T. Tamura and N. Sato, Maruishi Seiyaku Co., Ltd., Japan, in: *Bokin Bobai Shi* 6: 10 - 16 (1978)) JCL-ICR male mice were given a single dose of 0, 30 or 60 mg/kg glutaraldehyde (25% diluted in distilled water to 0.5%), formaldehyde at 70 mg/kg for comparison, ethylmethane sulfonate (300 mg/kg) as positive control, 10 males per group. Doses with glutaraldehyde were stated to be 1/10 and 1/5 of the LD50. Untreated females were mated 1:1 with males for 4 days. Males were mated with females, 4 days per time period, for 6 weeks. Females were examined on the 12-13th day of presumed gestation. The parameters measured included corpora lutea count, total implants, preimplantation loss, live implants, early and late deaths. Exposure to EMS resulted in an increase in lethality in the first 2-3 weeks. The results with glutaraldehyde were stated in the text to be considered negative overall. Due to the poor quality of the tables of data, it was not possible to evaluate the results.
UNACCEPTABLE (published study with no individual data, poor quality tables, inadequate number of males per group for mating). Not upgradeable. (Berliner, 4/22/85 and Gee, 7/23/99).

006 920372, brief results summary.

008 031807, 031808, brief results summaries.

008 031806, brief results summary.

DNA DAMAGE

** 151 131908: Vergnes, J. S. and E. R. Morabit, "Ucarcide® Antimicrobial 250 (Glutaraldehyde, 50% aqueous solution): *In Vivo* Blood Micronucleus Test with Swiss-Webster Mice". (Bushy Run Research Center (BRRC), Laboratory Project ID 91U0101, 2/26/93.) Ucarcide® Antimicrobial 250, purity 50% glutaraldehyde, was administered via single dose peroral intubation at doses of 0, 80, 160, or 250 mg/kg to 5 Swiss-Webster mice/sex/group for low and mid doses and 8/sex for the high dose. Doses were not corrected for glutaraldehyde content. Positive control was triethylenemelamine at 24 hours only. Blood samples were collected at 30, 48 and 72 hours post treatment by tail nicking. Micronuclei in 1000 PCEs per animal were scored and the number of PCE/1000 NCE were reported. Males appeared unkempt, especially in mid and high dose groups. There were no significant increases in the incidences of micronucleated PCEs. Analysis of dosing material not reported. ACCEPTABLE (Kishiyama and Gee, 7/17/2000).

50255-234 178366 "Toxicology and carcinogenesis studies of glutaraldehyde (CAS No. 111-30-8) in F344/N rats and B6C3F_1 mice " (National Toxicology Program, NTP No. 490, NIH Publication No. 99-3980, Battelle Northwest Laboratories, B. J. Chou, Principal Investigator, September, 1999) Section: **Micronuclei in bone marrow of male mice, single injection.** Study conducted at Environmental Health Research and Testing, Inc. Male mice given a single intraperitoneal injection for Trial 2 of the chromosomal aberration assay [see 1-liner above under Chromosome effect] were also examined for micronuclei in the polychromatic erythrocytes at 36 hours. The number scored per animal was not stated [1000 implied]. Doses of glutaraldehyde were 0 (saline), 15, 30, 50 and 60 mg/kg. Numbers of animals per dose were 5, 5, 4, 5 and 5, control through high dose. Mitomycin C was the positive control and functional. The results indicated the mean values of micronucleated PCEs/1000 PCEs was 0.70 (control), 1.5 (15 mg/kg), 1.38 (30 mg/kg), 1.90 (50 mg/kg) and 1.6 (60 mg/kg) with a statistical significance of $p = 0.028$ by a one-tailed trend test. The investigators considered a $p < 0.025$ to be indicative of a positive response (citation: Integrated Laboratory Systems (ILS), 1990, Micronucleus Data Management and Statistical Analysis Software, Version 1.4, Research Triangle Park). Therefore, these results were judged as "equivocal" (page 00050). UNACCEPTABLE (data presented as one page of means of results, use of males only with no justification). No worksheet. Gee, 1/18/01)

50255-234 178366 "Toxicology and carcinogenesis studies of glutaraldehyde (CAS No. 111-30-8) in F344/N rats and B6C3F_1 mice" (National Toxicology Program, NTP No. 490, NIH Publication No. 99-3980, Battelle Northwest Laboratories, B. J. Chou, Principal Investigator, September, 1999) Section: **Micromuclei in bone marrow of male mice – three injections.** Study conducted at Environmental Health Research and Testing, Inc. Data presented in a single page of summary results

with the protocol by citation (Shelby, M. D. *et al.*, Environmental and Molecular Mutagenesis 21: 160 – 179 (1993)). Male mice were given three intraperitoneal injections (timing was not stated) at doses of glutaraldehyde of 0 (saline), 5, 10 and 20 mg/kg, five mice per dose, with mitomycin-C as the positive control. The citation states that the injections are made on three consecutive days with harvest 24 hours after the last injection. The number of polychromatic erythrocytes scored per animal was not given but 1000 was implied. Again, the citation states that two slides are prepared per mouse with a total of 2000 PCEs scored for micronuclei (page 168 of reference) per animal. There were two trials. In neither trial was there a significant increase in the incidence of micronuclei with treatment. The conclusion was that the assay was negative as conducted. The positive control was functional. UNACCEPTABLE (report was one page of summary data, use of males only with no justification). No worksheet. (Gee, 1/18/01)

50255-234 178366 "Toxicology and carcinogenesis studies of glutaraldehyde (CAS No. 111-30-8) in F344/N rats and B6C3F_1 mice" (National Toxicology Program, NTP No. 490, NIH Publication No. 99-3980, Battelle Northwest Laboratories, B. J. Chou, Principal Investigator, September, 1999) Section: **Micronuclei in peripheral blood erythrocytes after 13 weeks.** Study performed at SRI International. Data were presented as a one-page summary. [It is unclear if these mice were from record no. 131901] Mice, 10/sex/group, were exposed to glutaraldehyde at 0 (chamber control), 62.5, 125, 250 or 500 ppb, presumably for 13 weeks. Protocol cited as following MacGregor, J. T. *et al.*, Fundam. Appl. Toxicol. 14: 513 – 522 (1990). Urethane in drinking water of three males served as the positive control. There was no increase in micronucleated normochromatic erythrocytes per 1000 NCEs with dose. The positive control was functional. UNACCEPTABLE due to missing information. (Gee, 1/18/01)

** 145 131242: SanSebastian, J. R. "*In Vivo* Micronucleus Test with Sepacid GA 50 in Mouse Bone Marrow Erythropoietic Cells". (Pharmakon Research International, Inc., PH 309-BS-001-93, 5/25/94.) Sepacid GA 50, was administered via a single intraperitoneal injection at concentrations of 0, 2, 10, or 20 mg/kg to 5 CD-1 albino mice/sex/group. Scheduled sacrifices were at 24, 48 and 72 hours after treatment. Positive control, TEM, was evaluated at 24 hours only. An increase in micronucleated PCE frequency observed in the initial assay was not repeated; therefore, Sepacid GA 50 was considered non-genotoxic. ACCEPTABLE. (Kishiyama and Gee, 7/21/2000).

131 114663 "Glutaraldehyde (50%) *In Vitro* Mutagenesis Studies: 3 Test Battery. UDS test ". (R. S. Slesinski, Carnegie-Mellon University, Project Report 43-16, 1/28/80.) Glutaraldehyde, 50.7% ai, was evaluated for DNA damage to rat hepatocytes at concentrations of 0.1, 1, 3, 6, 10, 30, 60, 100 x 10^{-4}% (v/v) and at 0.1, 1, 3, 10, 30, and 100 x 10^{-5}% (v/v) in trials 1 and 2, respectively. There were duplicate cultures per concentration. The incorporation of radioactivity into nuclei and DNA was quantitated by liquid scintillation spectrometry but procedures not described. Data presented as the mean $\pm$ SD for nuclei and for DNA. DNA recovery after precipitation was not quantitated. UNACCEPTABLE. Not upgradeable (high background incorporation into control samples, positive controls not statistically significant, only 2 cultures per concentration, missing protocol information, inadequate presentation of the results, others). (Berliner, 1/28/91; Kishiyama and Gee, 7/27/99).

032 016880. Duplicate of 131 114663 above.

GENERAL GENOTOXICITY

134 115342 "Mutagenicity Evaluation of Glutaraldehyde in a Battery of *in vitro* bacterial and Mammalian Test Systems." (Slesinski, R. S. *et al.*, published in: Food Chem. Toxic. 21: 621 - 629 (1983) from Bushy Run Research Center, 1982) Summary data from four tests: *Salmonella typhimurium*, CHO/HGPRT gene mutation assay, CHO sister chromatid exchange assay and primary rat hepatocyte unscheduled DNA synthesis assay. Under the conditions of the assays, all were negative for genotoxicity. Glutaraldehyde used was approximately 50% aqueous solution. *Salmonella typhimurium* assay: Strains TA1535, TA1537, TA1538, TA98 and TA100 were tested with and without rat liver activation by plate incorporation with three plates per concentration on each of two days at 0 (water), 0.15, 0.5, 1.5, 5.2, 15.4 and 51.6 (toxic) ug/plate without activation and 0, 0.5, 1.5, 5.2, 15.4 and 51.6 ug/plate with activation. No induction of revertants. CHO/HGPRT: CHO-K_1-BH_4 cells were exposed with and without rat liver activation for 5 hours followed by 7 days for expression. Mutation frequency was determined with 6-thioguanine. Concentrations ranged from 2.6 to 40.8 (toxic) uM without activation and 0.03 to 40.8 uM with activation. Results were negative with cytotoxicity at higher concentrations. Sister chromatid exchange assay: CHO cells were exposed for 5 hours without activation or 2 hours with activation followed by 30 - 32 hours in the presence of BrdU. Concentrations were 0 (water), 0.6, 1.3 and 2.5 uM. Results were negative. Unscheduled DNA synthesis: Hepatocytes were isolated from Hilltop-Wistar rats and exposed for 2 hours in two separate trials. UDS was determined by the incorporation of ^{3}H-thymidine as measured by liquid scintillation counting of DNA precipitated from nuclei. Results were reported as dpm/10^6 viable cells and compared with water controls. Concentrations ranged from 0.05 to 51 uM in the two trials. Results were negative. No worksheet. (Gee, 7/25/00)

NEUROTOXICITY

Not required at this time.

033 016876 "On the specific molecular configuration of neurotoxic aliphatic hexacarbon compounds causing central-peripheral distal axonopathy." (Peter S. Spencer, M. C. Bischoff and H. H. Schaumburg, in: *Toxicology and Applied Pharmacology* 44: 17 - 28 (1978), from Albert Einstein College of Medicine) Young Sprague-Dawley rats were given one of a series of 10 hydrocarbon derivatives in drinking water. Glutaraldehyde, 0.1%, 0.25% and 0.5% , was included. Exposure lasted for 11 weeks with 3 per dose group. At termination, animals were sacrificed and perfused with paraformaldehyde and 5% glutaraldehyde. Tissues from the spinal cord and posterior tibial nerve were sampled, these areas having been shown to exhibit early changes in distal axonopathies. Tissues from those exposed to glutaraldehyde in drinking water were "indistinguishable" from controls. Glutaraldehyde was included because of its ability to cross-link proteins. UNACCEPTABLE (a publication lacking in adequate details.) (Berliner, 4/23/85 and Gee, 7/23/99).

006 920372 Brief results summary.

SUPPLEMENTAL STUDIES

149 131902 Nachreiner, D. J. and D. E. Dodd. "Ucarcide® Antimicrobial 250 Acute Vapor Inhalation Toxicity Test in Rats" (Bushy Run Research Center, Laboratory Project ID 53-8. November 6, 1990). Ucarcide® Antimicrobial 250, 50.9% ai, was administered via a single 4 hour whole body inhalation exposure at concentrations of 3 (static), 14.5 or 16.3 (dynamic bubble) ppm to 5 Sprague-Dawley albino rats/sex/group . On day of treatment, blepharospasm was observed for all treated animals and in addition, periocular, perioral, and/or perinasal wetness and encrustation, and audible respiration were observed for the mid and high dose groups. No other treatment related effects reported. SUPPLEMENTAL STUDY. (Kishiyama and Gee, 8/23/99)

** 50255 - 152 131918 Myers, R. C. And S. M. Christopher " UCARCIDE® antimicrobial 250: Acute peroral toxicity study in the rat" (Bushy Run Research Center, ID 54-145, 1/9/92) Ucarcide® containing 50% glutaraldehyde was given by oral intubation to 5 per sex per dose at 100, 200 or 400 mg/kg to males and 100, 141 or 200 mg/kg to females as aqueous dilutions. The doses were not adjusted for the 50% content of glutaraldehyde. Mortality was: Males, 0/5, 1/5 and 5/5 with increasing dose; females: 0/5, 2/5 and 4/5 with increasing dose. LD_{50} for males = 246 (179 - 339) mg/kg; females = 154 (116 - 206) mg/kg; combined = 200 (157 - 255) mg/kg. Clinical signs included sluggishness, piloerection, red crust on perinasal fur at 400 (males) and 200 (females). At 100 mg/kg in males, there were no signs of toxicity but in females, 1 showed sluggishness, 2 had trace amount of blood in the urine but these animals recovered by day 4. Observation was for 14 days. Gross necropsy findings included red lungs, glandular portion of the stomach dark maroon, hemorrhaged at the high dose in each sex. Category II. ACCEPTABLE. (Gee, 8/26/99)

032 018466 "Glutaraldehyde: Results of feeding in the diets of rats for 7 days" (Carnegie-Mellon Institute of Research, 8/29/75) Glutaraldehyde, 25%, was fed in the diet at 0, 0.1, 0.5, 1.0 or 2.0 gms of active ingredient per kg of body weight per day (actual doses of 0.1, 0.48, 1.02 and 1.63 g/kg/day) to Harlan-Wistar rats, 5/sex/dose, 30 days of age at start of treatment. Concentration in the diet as percentage was, for males, 0, 0.09, 0.44, 0.82 and 1.7 and for females, 0, 0.08, 0.36, 0.83 and 1.6. The effect on body weight and weight change, food consumption and liver and kidney weights were the only effects reported. There was no mortality. At the high dose, body weight change was depressed in both sexes. Based on the very limited data, the apparent NOEL = 1 g/kg body weight/day (body weight and food consumption depression). No worksheet. UNACCEPTABLE. Summary data with inadequate parameters measured. (Berliner, 4/19/85 and Gee, 7/20/2000)